ImmunoTools IT-Box-139 Award 2013

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Harnessing induced pluripotent stem cells for immunotherapy

Ever so often, organ and tissue transplantation is a lifesaving medical intervention. However, as the limited availability of organs and tissues is a great drawback, new sources have to be sought. With this in mind researchers have put more and more focus onto embryonic stem (ES) cells which confer great potential in regenerative medicine. ES cells are pluripotent cells, meaning that they can give rise to all types of tissues of the body, potentially allowing the generation of dopaminergic neurons for the treatment of Parkinsons disease or pancreatic beta cells for the treatment of type 1 diabetes. Furthermore, stem cells can be cultured and propagated indefinitely in the lab making them a potential inexhaustible source for tissue replacement therapy. As with human or animal derived whole organ and tissue transplants, a concern about the clinical applicability of ESC-derived tissues is their potential immunogenicity which may lead to graft rejection.

However, as the most recent Nobel Prize in Physiology or Medicine has indicated, regenerative medicine may have seen an interesting break through with the development of a method allowing patient skin cells to be ‘reprogrammed’ back to pluripotency. These induced pluripotent stem cells (iPSCs) can be differentiated into the tissues required by the patient. This method was thought to have overcome the barrier of immune rejection however recent evidence has shown that slight modifications occurring in the cells during reprogramming prevent these iPSCs from being accepted as ‘self’ tissue.

Considering this striking limitation and the fact that our laboratory has always been interested in immunology and stem cells, we have embarked on a journey of understanding and exploiting the master regulator of the immune system: the dendritic cell with its capacity to modulate and dictate between immunogenicity and tolerance. We have developed a protocol allowing the differentiation of patient-derived iPS cells into these dendritic cells (DCs). We are currently investigating the effect of a variety of different pharmacological agents and cytokines on the immunogenicity of DCs aiming at directing them away from immunogenic responses responsible for graft rejection and redirecting them towards a tolerogenic phenotype capable of the induction of graft acceptance. This may be an especially promising approach for the induction of tolerance towards a single antigen such as during

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enzyme replacement therapy as in cases such as haemophilia and lysosomal storage disease the induction of an immune response may neutralize treatment efficacy completely.

This is where the ImmunoTools *IT-Box-139.3* will enable us to investigate the immunogenicity of modulated DCs derived from patient iPS cells by looking at the induction of T cell responses and looking at the expression of costimulatory molecules, cytokines and MHC II by DCs which is one of many aspects we are going to look at.

I hope that I could convince you of how exciting and interesting this area of regenerative medicine is and that by controlling and redirecting the immune system a whole new range of treatments may become available to patients.

ImmunoTools *IT-Box-139.3* for **Alison Jane Leishman** includes 100 antibodies

FITC - conjugated anti-human CD1a, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD9, CD11a, CD11b, CD14, CD15, CD16, CD18, CD19, CD21, CD25, CD29, CD36, CD41a, CD43, CD45, CD45RA, CD46, CD52, CD53, CD54, CD58, CD62p, CD63, CD69, CD71, CD80, CD86, CD95, CD235a, HLA-ABC, HLA-DR, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE - conjugated anti-human CD2, CD3, CD4, CD8, CD11b, CD14, CD15, CD18, CD19, CD20, CD21, CD22, CD27, CD33, CD34, CD37, CD38, CD40, CD42b, CD45, CD45RB, CD50, CD72, CD95, CD105, CD147, CD177, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE/Dy647 -tandem conjugated anti-human CD45

APC -conjugated anti-human CD3, CD4, CD7, CD8, CD10, CD11c, CD14, CD16, CD19, CD27, CD37, CD40, CD44, CD56, CD59, CD61, CD62L, CD62P, CD69, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V DETAILS